

REMARKS

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has rejected Claim 2 as being indefinite under 35 U.S.C. § 112, second paragraph, for reciting a “means” for performing a specified function without reciting a structure in support of said means. Applicant submits that Claim 2 is definite in that it recites structure with sufficient distinctness in the claims and further in view of the specification.

Specifically, claim 2 recites two structures—B and B’, which are set forth in Claim 1 as being “independently bulky groups,” which sets forth a structural requirement. Further, the placement and orientation of the bulky groups are also set forth in Claim 1. The specification describes “bulky groups” as “branched or unbranched alkyl groups of from 3 to 10 carbons, as well as aromatic groups.” See pg. 8, lines 3-5. Based on this description in conjunction with the clear limitations set forth in the claims, Claim 2 clearly recites the structures that provide the specified function, i.e. steric hindrance of the counter enantiomer. Reciting these structures with further specificity would require naming a limited number of particular substituent groups, which would unduly restrict the scope of the invention. In the absence of relevant prior art, Applicant is entitled to as broad a scope as is supported by the specification. Claim 2 recites the structures that provide the specified function and that recitation is supported by the specification. Applicant therefore submits that the rejection of Claim 2 should be withdrawn. Reconsideration is respectfully requested.

Rejections under 35 U.S.C. § 103

The Examiner has rejected Claims 1-36 as obvious in view of Bradley et al (1990, J Org Chem 55:3129-3132) and/or Zhang et al (1997, Chem Rev 99:3313-3361) in view of Cram (U.S. Patent No. 4,001,279). The Applicant submits that the Examiner has not established a *prima facie* case of obviousness for the reasons stated below.

Standard for Establishing Prima Facie Case for Obviousness Under 35 U.S.C. § 103

To establish a *prima facie* case for rejecting an invention as obvious under 35 U.S.C. §103, three criteria must be met: (a) the prior art references relied upon, or general knowledge

available to one skilled in the relevant art, must contain some motivation for one skilled in the art to modify or combine those references; (b) the modification or combination proposed must have a reasonable expectation of success; and (c) the references, when combined, must teach or suggest all of the limitations of the present invention. MPEP §2143. The burden for meeting all of these criteria rests upon the Examiner. MPEP §2142. Applicant submits that the Examiner has not established a *prima facie* case for rejection of the present invention under §103, because the references relied upon do not contain the requisite motivation to combine the references, and further, because all of the claim elements are not present even if the references are properly combined.

Claimed Invention

The present invention provides compositions for selectively binding a preferred target enantiomer over its counter-enantiomer, as well as methods for separating said enantiomers using such compositions. These compositions and methods provide a diketo- and pyridine-containing chiral crown macrocycle that includes two bulky groups that are each attached to chiral carbons of the macrocycle, such as that shown in Figure 1 of the disclosure. These bulky groups contribute to the enantiomeric selectivity of the macrocycle by providing a steric barrier that hinders the counter-enantiomer from complexing thereto. The macrocycle is attached to the solid support and the structure is coated with a hydrophobic organic solvent coating.

Bradshaw and/or Zhang Reference(s) in view of Cram

The Bradshaw and Zhang articles discuss various structures for chiral macrocyclic ligands and various properties thereof as related to enantiomeric recognition and complexing capacity. These properties were described using data from analyses including calorimetry, NMR spectroscopy, and various types of mass spectrometry. Among the structures described are diketo- and pyridine-containing crown macrocycles.

The Examiner has stated that it would be obvious to one of ordinary skill in the art to modify Bradshaw and/or Zhang to include the solid support attachment described in Cram. To establish a *prima facie* case of obvious, the references themselves must contain a motivation for

one skilled in the art to combine them. The Examiner's opining without supporting documentation on which to base such an opinion is not permissible. Moreover, the motivation must not come from the Applicant's disclosure, as this would constitute an impermissible hindsight construction. The Applicant submits that there is no motivation in Bradshaw and/or Zhang to attach the macrocycles claimed in the present invention to a solid support, and further, to coat the solid support with an organic hydrophobic solvent coating. Bradshaw and Zhang are primarily concerned with the enantiomeric recognition properties of macrocycles having various structures and substituents. In fact, Bradshaw specifically states that "[w]e have shown that the pyridine-crowns form strong complexes with protonated organic amines . . . [and that t]he present paper describes the synthesis of new chiral pyridono-crown compounds." See Bradshaw at 3130. No mention or suggestion of attaching these specific compositions to solid supports is provided. Analyzing recognition capability in this context did not require or involve non-chromatographic separations using organic hydrophobic solvent-coated solid supports having attached macrocycles as claimed in the independent claims of the present application.

The Applicant submits further that there is no motivation suggested in Cram to attach the macrocycles of Bradshaw and Zhang to a solid support. Cram teaches chiral multiheteromacrocycles that include oxygen and binaphthyl unit, from which two pairs of ortho-positioned side chains arise, one pair (designated X) is proximal to the macrocycle, while the other pair (designated Y) are located distal to the macrocycle. The binaphthyl unit in Cram is an essential element to the compositions disclosed therein, in that it serves three functions: (1) it provides, via its X side chains, a steric barrier that hinders a particular enantiomer of a guest molecule from complexing with the macrocycle; (2) it acts as a hinge, in that variation in the dihedral angle between the planes of each naphthalene causes the diameter of the space within the macrocycle to vary accordingly; and (3) it provides, via its Y side chains, a means of tethering the macrocycle to a solid support.

Therefore, the binaphthyl unit taught in Cram is central both to its enantiomeric recognition and to its attachment of the macrocycles to a solid support. Applicant submits that one skilled in the art in possession of both the teaching in Bradshaw and/or Zhang as well as Cram would not be motivated to make the combination claimed by the Applicant. As stated

above, Bradshaw and Zhang do not suggest the attachment of the presently claimed macrocycles to a solid support. Furthermore, one skilled in the art would view the teaching in Cram as incompatible with the enantiomeric recognition functionality of the macrocycles in Bradshaw and Zhang. The ligands of Cram are of a completely different type than those described in Bradshaw and/or Zhang. In Bradshaw and Zhang, the steric barrier that contributes to the chiral selectivity of the macrocycle is provided by bulky substituents that are bound directly to its crown structure. This stands in contrast to the macrocycles provided in Cram, where the steric barrier is provided by a side chain substituent of the binaphthyl unit.

In addition to the lack of motivation to combine, assuming *arguendo* that the references were combined properly, neither reference teaches or suggests the use of a hydrophobic organic solvent coating which coats the solid support. To begin, as Bradshaw and Zhang do not teach of the attachment of these types of ligands to solid supports at all, by definition they cannot teach the coating of such compositions. Further, Cram also does not teach of the use of such a coating. To illustrate, claim 22 sets forth a bind-release non-chromatographic separation method, where Cram teaches chromatography. The processes set forth in claims 22 and 36 do not describe or read on traditional chromatography, and this distinction is important for the Examiner to understand. The present method claims require removal of the source solution from contact with the composition, contacting the composition with a receiving solution, and recovering the target enantiomer. Conversely, chromatography utilizes a mobile phase where the target composition merely moves more slowly down a column than other mobile phase constituents. Thus, chromatography is not a full bind and full release system. Further, the composition of claim 1 is particularly adapted for use in this type of a method (non-chromatographic separation). Cram is about chromatography, and thus is fundamentally compositionally different (e.g., Cram does not use a coating) and fundamentally used differently (e.g., Cram teaches of a chromatography method). Reconsideration of the claims is respectfully requested on these grounds.

In light of the foregoing, the Applicant submits that the primary references cited by the Examiner to not suggest a motivation for one skilled in the art to combine them with Cram or vice versa. Further, even if combined, all of the claim limitations are not present in the cited combination. Therefore, these references do not support a *prima facie* case of obviousness, and

Applicant requests that this rejection be withdrawn.

CONCLUSION

In light of the above, Applicant respectfully submits that pending claims 1-36 are in condition for allowance. Therefore, Applicant requests that the rejections and objections be withdrawn, and that the claims be allowed and passed to issue. If any impediment to the allowance of these claims remains after entry of this Amendment, the Examiner is strongly encouraged to call the undersigned at (801) 566-6633 so that such matters may be resolved as expeditiously as possible.

The Commissioner is hereby authorized to charge any additional fee or to credit any overpayment in connection with this Amendment to Deposit Account No. 20-0100.

DATED this 13th day of October, 2005.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Gary F. Oakeson", is written over a horizontal line.

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